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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,649	01/28/2002	Johannes Gerdes	3276.1000000	2383

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,649	GERDES ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-43 and 46-48* is/are pending in the application.

4a) Of the above claim(s) *32-38, 40-42 and 48* is/are withdrawn from consideration.

5)☒ Claim(s) *27* is/are allowed.

6)☒ Claim(s) *25,26,28,30,39,43,46 and 47* is/are rejected.

7)☒ Claim(s) *29 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 04/24/03 (Paper No. 13), is acknowledged.

2. Claims 25-43 and 46-48 are pending.

3. Claims 32-38, 40-42 and 48 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 25-31, 39, 43, and 46-47 are under consideration in the instant application.

5. In view of the amendment filed on 04/24/03 (Paper No. 13), only the following rejections remained.

6. The declaration of biological deposit and the statement under 37 C.F.R 1.806 and 1.808 concerning DSM Deposit No. ACC2388, filed 04/24/03 are sufficient to satisfy the requirement for the deposit of biological materials under 35 U.S.C. § 112, first paragraph.

7. The information disclosure statement (IDS) filed 4/24/03 fails to comply with 37 CRF 1.9(c) because it lacks the fee set forth in 37 CRF 1.17(p). It has been placed in the application file, but the information referred to therein has not been considered. Further, the entire documents were not found.

8. Formal drawings have been submitted on 4/24/03 (Paper No. 15), fails to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

9. The amendment to the specification filed on 4/24/03, to replace the paragraph at page 3, lines 27 through 34 fails to point out figure Number. Further, it appears that the figure contain two panels that must be identified in the Brief Description of the Drawings as "Figures 1A and 1B", after which each individual panel must be separately described. Correction is required.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 26 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the same reasons set forth in the previous Office Action, paper No. 11, mailed 11/20/02.

A. Claim 26 is indefinite in the recitation of "same binding properties". It is unclear what properties are contemplated.

Applicant's arguments, filed 4/24/03 (Paper No. 13), have been fully considered, but have not been found convincing.

Applicant amended the claim to recite "same binding properties", however, antibodies that bind to the same epitope have different antigen-binding sites and bind the epitope with different affinity. Therefore, it is unclear how to obtain such antibodies with the same binding properties.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 25, 26, 28, 30, 39 and 43 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuruga et al (of record) in view of Harlow et al 1989 and U.S. Patent 5,876,438 for the same reasons set forth in the previous Office Action, paper No. 11, mailed 11/20/02.

Applicant's arguments, filed 4/24/03 (Paper No. 13), have been fully considered, but have not been found convincing.

Applicant argues that Tsuruga et al teach away from producing monoclonal antibodies specific for human Mcm3. Further, Applicant argues that polyclonal antibodies are structurally and functionally different from the monoclonal antibodies. In particular, polyclonal antibodies do not possess the structural and functional specificity of monoclonal antibodies. A polyclonal antibody can bind a multiplicity of different epitopes on the immunizing antigen, while monoclonal antibodies bind to a specific epitope. Therefore, the monoclonal antibodies of the present invention are structurally and functionally different from the polyclonal antibody against HsMcm3 taught by Tsuruga et al.

However, it is unclear how Tsuruga et al teachings teach away from producing monoclonal antibodies specific for human Mcm3. Further, while the Examiner agree with applicant's assertion that polyclonal antibodies are structurally and functionally different from monoclonal antibodies and polyclonal antibody can bind a multiplicity of different epitopes on the immunizing antigen, while monoclonal antibodies bind to a specific epitope. However, antibodies that bind the same or nearly the same epitopes would meet the claimed antibody specificities. Furthermore, the issue is the obviousness for one ordinary skill in the art at the time of the invention was made to use the same HsMcm3 peptide taught by Tsuruge *et al* to make monoclonal antibodies as taught by the `500 patent.

Applicant further argues that Harlow et al reference is a laboratory manual that provides general methods for producing monoclonal antibodies and that Harlow et al do not teach or suggest producing a monoclonal antibody specific for human Mcm3. Applicant Argues that the `438 patent does not cure the deficiencies of the Tsuruga *et al* and the Harlow et al references. Moreover, no where taught in the `438 patent that monoclonal antibodies specific for human Mcm3 can be used in the intraocular devices, and the `438 patent does not teach or suggest producing a monoclonal antibody specific for human Mcm3. The `438 patent does not even mention human Mcm3.

However, specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA).

Applicant argues in conjunction with case law that the Examiner has not identified a suggestion in the prior art of the desirability of proposed combination of references. Further, combining the elements of separate references which do not themselves suggest the combination necessary to obtain a claimed invention is generally improper.

However, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin , 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). See MPEP 2145.

Furthermore, Applicant argues in conjunction with case law that *a prima facie* case of obviousness is established only if the teachings of the cited art would have suggested the claimed invention to one of ordinary skill in the art with a reasonable expectation of successfully achieving the claimed results. Applicant argues that both the suggestion and the reasonable expectation of success must be found in the prior art, not Applicants' disclosure.

However, obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousnes. In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). See MPEP 2143.02

Applicant argues that none of the cited references alone or in combination, would have suggested the claimed invention to one of ordinary skill in the art at the time the invention was made with a reasonable expectation of success. Applicant asserts that non of the cited references alone or in combination would have suggested monoclonal antibody specific for human Mcm3 to one of ordinary skill in the art at the time the invention was made with a reasonable expectation of success. Applicant continue to argue that none of the cited references, alone or in combination would have suggested a hybridoma cell line expressing a monoclonal antibody specific for human Mcm3 or process for producing a monoclonal antibody specific for human Mcm3 to one of ordinary skill in the art at the time the invention was made with a reasonable expectation of success. Further, Applicant argues that none of the cited references alone or in combination, would have suggested a diagnostic or pharmaceutical composition comprising a monoclonal antibody specific for human Mcm3 to one of ordinary skill in the art at the time the invention was made with a reasonable expectation of success. Applicant concludes that the cited references, either alone or in combination, would not have suggested the claimed invention to one of ordinary skill in the art, at the time the invention was made, with a reasonable expectation of success.

However, there is no objective evidence has been provided to indicate that the art known process of generating antibodies, including generating monoclonal antibodies for over the past 25 years, to antigens/polypeptides of interest would not be successful given the prior art teaching.

Applicant argues that even assuming, *arguendo*, that a prima facie case of obviousness exists, which it does not, the prima facie case of obviousness would be overcome by a showing of unexpected results. Applicant argues that the polyclonal antibodies are structurally and functionally different from monoclonal antibodies. Polyclonal antibodies do not possess the structural and functional specificity of monoclonal antibodies. The claimed monoclonal anti-Mcm3 antibody recognizes only one protein band at 105 kDa, while the polyclonal antibody recognizes both 105kDA protein band and additional protein bands with apparent molecular weight between 50 and 90 kDa. Additionally, Applicant have demonstrated the unexpected results that at antibody concentrations between 0.15 to 6 mg/L monoclonal anti-Mcm3 antibodies perform better than the polyclonal anti-MCm3 antibodies in detecting the presence of Mcm3 protein both in normal tissue and tumor tissue.

Applicant's reliance on unexpected results do not overcome clear and convincing evidence of obviousness. Also see Richardson-Vicks Inc. v. Upjohn Co., 44 USPQ2d 1181 (CAFC 1997). Further,
Harlow et al teach that the monoclonal antibodies stems from their specificity, homogeneity and ability to be produced in unlimited quantities. Therefore, one of skill in the art at the time of the invention was made would expect the monoclonal antibodies to have a single band that represent the molecular weight of protein of interest due to the single antigen-binding site of the monoclonal antibodies. Similarly, the better performance of the monoclonal antibodies to Mcm3 is considered inherent properties of the claimed anti-Mcm3.

13. Claim 46 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuruga et al (of record) in view of Harlow et al 1989 and U.S. Patent No. 4,281,061 for the same reasons set forth in the previous Office Action, paper No. 11, mailed 11/20/02.

Applicant's arguments, filed 4/24/03 (Paper No. 13), have been fully considered, but have not been found convincing.

Applicant argues that the Examiner has not identified a suggestion in the prior art of the desirability of the proposed combination of references. Applicant concluded that the rejection is improper.

However, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

Applicant argues that the teachings of the cited references, either alone or in combination, would not have established, to a reasonable degree of certainty, the monoclonal antibodies specific for human Mcm3 or diagnostic kit comprising a monoclonal antibody specific for human Mcm3 of the present invention. Applicant concluded that these references would not have suggested the claimed invention to one of ordinary skill in the art, at the time the invention was made, with a reasonable expectation of success.

However, there is no objective evidence has been provided to indicate that the art known process of generating antibodies, including generating monoclonal antibodies for over the past 25 years, to antigens/polypeptides of interest would not be successful given the prior art teaching.

14. Claim 47 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuruga et al (of record) in view of Harlow et al 1989 and U.S. Patent No. 4,281,061, as applied to claim 46 above, and further in view of U.S. Patent No. 6,316,208 for the same reasons set forth in the previous Office Action, paper No. 11, mailed 11/20/02.

Applicant's arguments, filed 4/24/03 (Paper No. 13), have been fully considered, but have not been found convincing.

Applicant argues that the Examiner has not identified a suggestion in the prior art of the desirability of the proposed combination of references. Applicant concluded that the rejection is improper.

However, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

Applicant argues that the teachings of the cited references, either alone or in combination, would not have established, to a reasonable degree of certainty, the monoclonal antibodies specific for human Mcm3 or diagnostic kits comprising a monoclonal antibody specific for human Mcm3 of the present invention. Applicant concluded that these references would not have suggested the claimed invention to one of ordinary skill in the art, at the time the invention was made, with a reasonable expectation of success.

However, there is no objective evidence has been provided to indicate that the art known process of generating antibodies, including generating monoclonal antibodies for over the past 25 years, to antigens/polypeptides of interest would not be successful given the prior art teaching.

15. Claim 27 is allowable.

16. Claims 29 and 31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
June 30, 2003

CHRISTINA CHAN
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